Gene regulatory network subcircuit controlling a dynamic spatial pattern of signaling in the sea urchin embryo.

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Public Summary:
The “identity” of any cell – how it behaves, the functions it serves – is determined by the combination of a vast number of genes that are actively expressed in that cell. The actual process by which a cell gains its identity, called “specification”, is similarly complex, involving many dozens or hundreds of genes. Specification also involves many “noisy” events, yet given the huge number of possibilities for mistakes to happen it is striking how highly reliable the process is at producing reproducible outcomes. We identified the network of regulatory interactions conferring reliability using the sea urchin embryo as a model. The process of regeneration must also involve highly robust mechanisms to respond to injury and to repair functional tissues. In the absence of reliable mechanisms, regeneration could instead become detrimental to the organism. This may underly the inability of some animals to regnerate complex tissues. Thus, the ability to identify the regulatory interactions conferring network reliability can be important to studies of regeneration in tissue that do not normally repair and regrow.

Scientific Abstract:
We dissect the transcriptional regulatory relationships coordinating the dynamic expression patterns of two signaling genes, wnt8 and delta, which are central to specification of the sea urchin embryo endomesoderm. cis-Regulatory analysis shows that transcription of the gene encoding the Notch ligand Delta is activated by the widely expressed Runx transcription factor, but spatially restricted by HesC-mediated repression through a site in the delta 5'UTR. Spatial transcription of the hesC gene, however, is controlled by Blimp1 repression. Blimp1 thus represses the repressor of delta, thereby permitting its transcription. The blimp1 gene is itself linked into a feedback circuit that includes the wnt8 signaling ligand gene, and we showed earlier that this circuit generates an expanding torus of blimp1 and wnt8 expression. The finding that delta expression is also controlled at the cis-regulatory level by the blimp1-wnt8 torus-generating subcircuit now explains the progression of Notch signaling from the mesoderm to the endoderm of the developing embryo. Thus the specific cis-regulatory linkages of the gene regulatory network encode the coordinated spatial expression of Wnt and Notch signaling as they sweep outward across the vegetal plate of the embryo.

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